DOCKET NO.: CP380G
Application No.: 10/789,604
Office Action Dated: June 23, 2006

PATENT

REMARKS

Following entry of the foregoing amendments, claims 1, 3 to 12, and 16 to 18 will be pending in the application. Claims 1, 3 to 9, 12, and 16 to 18 to have been amended, and claims 2 and 13 to 15 have been canceled, herein, without prejudice. No new claims have been added. Support for the amendments is found throughout the specification as originally filed. No new matter has been added.

Applicants respectfully request reconsideration of the rejections of record in view of the foregoing amendments and the following remarks.

Alleged Obviousness

Claims 1 to 13 and 16 to 18 have been rejected under 35 U.S.C. § 103(a) as allegedly obvious over Chinese Patent number CN 1079391 ("the 391 patent") in view of U.S. Patent No. 6,720,011 ("the Zhang patent") Shimotsuura, S., *Journal of Tokyo Dental College Society*, 1986, 86(8) 1237-1253 ("the Shimotsuura article"), and U.S. Patent No. 5,748,699 ("the Smith patent"). Applicants respectfully request reconsideration and withdrawal of the rejection because the Office has failed to establish *prima facie* obviousness.

To establish *prima facie* obviousness, the Patent Office must provide objective evidence that the prior art relied upon, coupled with the knowledge generally available in the art at the time of the invention, contains some suggestion or incentive that would have motivated those of ordinary skill in the art to modify a reference or to combine references. *In re Lee*, 61 U.S.P.Q.2d 1430, 1433 (Fed. Cir. 2002); *In re Fine*, 837 F.2d 1071, 1074, 5 U.S.P.Q.2d 1596, 1598 (Fed. Cir. 1998). And the proposed modification or combination of the prior art ***must have had a reasonable expectation of success***, determined from the vantage point of those of ordinary skill in the art, at the time the invention was made. *Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1209, 18 U.S.P.Q.2d 1016, 1023 (Fed. Cir. 1991).

"[W]hether a particular combination might be 'obvious to try' is not a legitimate test of patentability." *In re Fine*, 837 F.2d 1071, 1075 (Fed. Cir. 1988). "Obvious to try" situations arise where it might have been obvious to "explore a new technology or general approach that seemed to be a promising filed of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it." *In re O'Farrell*, 853 F.2d 894, 903 (Fed. Cir. 1988). *See also Hybritech Inc. v. Monoclonal*

Antibodies, Inc., 802 F.ed. 1367, 1380 (Fed. Cir. 1986)(stating that "At *most*, these articles are invitations to try monoclonal antibodies in immunoassays but do not suggest how that end might be accomplished.")(emphasis in original).

Upon review of the references cited in the Office action, those skilled in the art would not have reasonably expected at the time of the invention that a combination of arsenic trioxide and radiation could have been successfully used to treat colon, ovarian, renal, bladder, or prostate cancer in humans. At most, it might have been obvious to persons skilled in the art ***to try*** to use arsenic trioxide and radiation to treat such cancers, but much more is required to establish *prima facie* obviousness.

Upon review of the 391 patent, those skilled in the art would not have reasonably expected that arsenic trioxide could have been successfully used to treat colon, ovarian, renal, bladder, or prostate cancer in humans. The 391 patent indicates that the use of arsenic preparations had been reported in the literature for the treatment of skin and cervical cancers. The patent then generalizes these findings by stating that arsenic preparations have been used for the treatment of "body surface and cavity cancers," but further states that the arsenic preparations described in the literature have a "range of application [that] is quite narrow, and they are still unable to touch upon in vivo cancer tumors....Some of the dosage forms are not advantageous to industrialized mass production, some are not convenient to use, and for some it is difficult to control the quality between batches during production."[1] The patent indicates that the invention therefore involves the development of new arsenic-containing formulations and dosage forms to be used for the treatment of body surface and body cavity tumors.[2]

The 391 patent, however, is limited to a description of how the arsenic formulations and dosage forms are prepared, and provides no indication that the arsenic formulations are efficacious for cancer treatment. Based upon the efficacy of arsenic preparations for the treatment of skin and cervical cancer reported in the literature, the patent generalizes that the described preparations can be used to treat any and all body surface and body cavity cancers. Those skilled in the art recognize, however, that such generalizations are unwarranted. Skilled artisans would have appreciated at the time of the invention that the efficacy of a particular anti-cancer agent against a specific type of cancer, such as cervical cancer, was not predictive of its efficacy against other types of cancers, such as colon, ovarian, renal, bladder, and prostate

[1] *See* page 7.
[2] *Id.*

cancers. It was understood that "[i]ncreasingly disease-specific therapies are being developed that will have optimum application for only one tumor type, although representing ineffective and toxic treatment for others."[3] Indeed, the therapeutic agents most commonly used to treat cancers at the time of the invention (and at present, as well) were effective only against specific types of cancers, and generally did not exhibit broad efficacy against numerous cancer types.[4] Accordingly, those skilled in the art at the time of the invention would not have reasonably expected that arsenic trioxide could have been successfully used to treat colon, ovarian, renal, bladder, or prostate cancer in humans just because it had been reported to have efficacy in humans against skin and cervical cancers. Although those skilled in the art might arguably have considered trying to use arsenic trioxide to treat cancers in humans other than skin and cervical cancers, the results of doing so could not have been predicted with a reasonable degree of certainty. Accordingly, based upon the teachings of the 391 patent, those skilled in the art at the time of the invention would not have reasonably expected that arsenic trioxide could have been successfully used to treat colon, ovarian, renal, bladder, and prostate cancers in humans.

The Zhang patent, Shimotsuura article, and Smith patent do not compensate for the deficiencies of the 391 patent. For example, the Zhang patent describes arsenic trioxide compositions[5], but fails to provide any guidance whatsoever as to the efficacy of the compositions against colon, ovarian, renal, bladder, or prostate cancer treatment. The patent states that arsenic trioxide can be used to treat leukemia, hepatoma, and lymphoma.[6] Notably, the patent's single working example describes the use of arsenic trioxide compositions for the treatment of a particular type of leukemia (acute promyelocytic leukemia).[7] In addition, the patent's description of the effect of the described arsenic trioxide compositions on cancer cells is limited to a description of its effect on leukemia cells:

> Laboratory experiments indicate that the composition shows a strong abruptive effect on the membranes of leukemic cells. It also inhibits DNA/RNA synthesis in such cells, reduces the rate of proliferation of leukemic cells and destroys the leukemic cells.[8]

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[3] *Medical Oncology*, Calabresi, P., *et al.*, eds., 1985, Macmillan Publishing Company, page 257 (copy enclosed as Exhibit A).
[4] *Id.* at 295-297 (copy enclosed as Exhibit A).
[5] "The present invention is directed to an intravenous drip composition for the treatment of cancers. The cancers treatable include leukemia, hepatoma and lymphoma." (col. 1, lns. 33 to 35).
[6] *See* col. 1, ln. 35.
[7] *See* col. 2, ln. 59 to col. 3, ln. 27.
[8] See col. 2, lns. 23 to 27.

The Shimotsuura article fails to describe or suggest the treatment of colon, ovarian, renal, bladder, or prostate cancer with arsenic trioxide. Rather, the article describes the efficacy of arsenic trioxide in a mouse sarcoma model and indicates that arsenic trioxide was only efficacious when it was coadministered with an antidote. Although the Office action asserts that the article teaches that "antineoplasmic [*sic*] actions of arsenic trioxide are primarily achieved by DNA composition blockage,"[9] the article states that the DNA composition blockage occurred in the S-180 (sarcoma) cells transplanted into the mice, and does not teach that DNA composition blockage occurs in cancerous cells other than sarcoma cells:

> From above results, As_2O_3 is considered that can increase life span of the mouse by blocking DNA composition of S-180 cells and protein composition.[10]

The Smith patent describes a device that can be used to deliver radiation to tissues that line body cavities, such as the bladder and colon, and states that the device can be used to treat tumors in such cavities. The patent fails to teach or suggest, however, that bladder and colon cancer can be treated with arsenic trioxide.

The references cited in the Office action thus fail to teach or suggest that a combination of arsenic trioxide and radiation can be successfully used to treat colon, ovarian, renal, bladder, or prostate cancer in humans. Rather, the references suggest that radiation can be used to treat bladder and colon cancer, and teach that arsenic trioxide has been used in humans to treat unspecified "skin cancer," cervical cancer, and acute promyelocytic leukemia. The references suggest that arsenic trioxide may be effective against hepatoma and lymphoma, and may be used to treat sarcomas when administered in conjunction with an antidote. The combined teachings of the cited references thus fail to suggest treatment of colon, ovarian, renal, bladder, and prostate cancer with a combination of arsenic trioxide and radiation.

The Office action asserts that "it would have been obvious from the disclosure of CN 1079391 that cancers such as bladder cancer (a body cavity cancer) and related cancer such as cervical cancer (another body cavity cancer) are clearly suggested from said disclosure."[11] However, as discussed above, even if those skilled in the art would have been motivated to attempt to treat body cavity cancers with a combination of arsenic trioxide and radiation based upon the teachings of the cited references, they would not have had a reasonable expectation of

[9] Office action dated June 23, 2006, page 4.
[10] Page 20 of the English translation.
[11] Office action dated June 23, 2006, page 6.

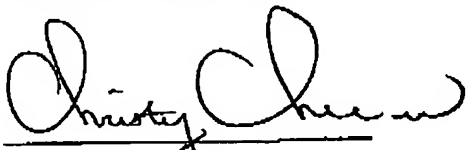
success for such an endeavor. The Office action appears to be asserting that those skilled in the art would have been motivated to use a combination of arsenic trioxide and radiation to treat any type of body cavity cancer. Due to the nature of cancer, and methods for its treatment and management at the time of the invention, however, those skilled in the art would not have reasonably expected that an agent shown to be effective against one type of body cavity cancer could have been successfully used to all body cavity cancers in humans.

Applicants respectfully submit, therefore, that the Office action has failed to establish *prima facie* obviousness, and Applicants, accordingly, respectfully request withdrawal of the rejection.

Conclusion

Applicants believe that the foregoing constitutes a complete and full response to the Office action of record. Accordingly, an early and favorable action is respectfully requested.

Respectfully submitted,



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